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(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

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(54) Title: KINASE INHIBITORS

(57) Abstract: The invention relates to inhibitors of kinases, compositions comprising the inhibitors, and methods of using the inhibitors and inhibitor compositions. The inhibitors and compositions comprising them are useful for treating disease or disease symptoms. The invention also provides for methods of making kinase inhibitor compounds, methods of inhibiting kinase activity, and methods for treating disease or disease symptoms.

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D239/47 C07D239/88 C07D239/93 C07D239/95 A61K31/513
A61K31/517 A61P11/00 A61P25/00 A61P35/00 A61P37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 048 250 A (THE UPJOHN CO.) 10 December 1980 (1980-12-10) page 25, line 35 - line 41 page 26, line 26 - line 56 claims	1-6,8
X	US 4 308 272 A (W. WIERENGA ET AL.) 29 December 1981 (1981-12-29) column 2, line 21 - line 28; claim 1	1-6,8
X	WO 98 25596 A (PHARMACIA & UPJOHN CO.) 18 June 1998 (1998-06-18) page 8, line 31 -page 99, line 23; claims 1,3,8	1-6,8
X	US 4 689 328 A (I. H. HALL ET AL.) 25 August 1987 (1987-08-25) claims 1-8; table 1	1,2,6,8

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 July 2000	24. 10. 00

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hass, C

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 15, no. 154 (C-0825), 18 April 1991 (1991-04-18) & JP 03 031267 A (MORISHITA PHARMACEUT CO LTD), 12 February 1991 (1991-02-12) abstract	1,2,6,8
X	PATENT ABSTRACTS OF JAPAN vol. 11, no. 38 (C-401), 4 February 1987 (1987-02-04) & JP 61 205260 A (ZERIA SHINYAKU KOGYO KK), 11 September 1986 (1986-09-11) abstract; formulae I, II	1-6,18, 19
X	V. J. RAM ET AL.: EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, vol. 25, no. 6, 1990, pages 533-8, XP000929367 page 534, compounds 21 and 3 to 14	1-6,18, 19
X	S. A. ABDEL-AZIZ ET AL.: PHOSPHORUS, SULFUR AND SILICON, vol. 113, no. 1-4, 1996, pages 67-77, XP000864775 page 68, compounds (1) and (4); page 70, compound (10)	1-6,18
X	N. RASHED ET AL.: JOURNAL OF THE CHINESE CHEMICAL SOCIETY, vol. 40, no. 4, 1993, pages 393-7, XP000864792 Taipei page 394, scheme I, compounds 1, 5; page 395, compound 5	1-6,18
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	V. J. RAM ET AL.: JOURNAL FÜR PRAKTISCHE CHEMIE, vol. 332, no. 5, 1990, pages 629-39, XP000864779 page 631, scheme 2, compounds 14 a-d; page 630, scheme 1, definition of QR ---	1-6
X	V. J. RAM: JOURNAL FÜR PRAKTISCHE CHEMIE, vol. 331, no. 6, 1989, pages 893-905, XP000864780 page 894, compounds 6-17 ---	1-6
X	V. J. RAM: ARCHIV DER PHARMAZIE, vol. 323, no. 11, 1990, pages 895-9, XP000864784 scheme 1 ---	1-6
X	N. H. ESHBA: ALEXANDRIA JOURNAL OF PHARMACEUTICAL SCIENCE, vol. 9, no. 1, 1995, pages 31-4, XP000864773 page 32, scheme 1, first formula, compounds VII-IX ---	1-6
X	F. A. ATTABY ET AL.: ARCH. PHARMACAL RES., vol. 20, no. 6, 1997, pages 620-8, XP000864772 page 625, compounds 1a-c, 2a-c; page 627, compounds 20a-c, 27a-f, 24a-c ---	1-6
X	S. KAMBE ET AL.: SYNTHESIS, no. 4, 1979, pages 287-9, XP000929368 page 288, compounds 4a, 8 ---	1-6
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Interna al Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	S. M. HUSSAIN ET AL.: JOURNAL OF HETEROCYCLIC CHEMISTRY, vol. 22, no. 1, 1985, pages 169-71, XP000929371 page 169, compounds IV, VI; page 170, compound IX	1-6
X	A. M. EL-REEDY ET AL.: JOURNAL OF HETEROCYCLIC CHEMISTRY, vol. 26, no. 2, 1989, pages 313-6, XP000929372 page 313, compounds I, III	1-6
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P,X	J. M. PARMAR ET AL.: INDIAN JOURNAL OF CHEMISTRY, vol. 38b, no. 4, April 1999 (1999-04), pages 440-4, XP000864783 page 441, compound 1	1-6
X	J. F. W. KEANA ET AL.: JOURNAL OF ORGANIC CHEMISTRY, vol. 41, no. 12, 1976, pages 2124-9, XP002143538 page 2125, chart I, compound 3	1,2,6
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 10-15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6, 8(partly), 9(partly), 10-19

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6, 8(partly), 9(partly), 10-19

   Pyrimidine derivatives of the formula as defined in claim 1, their pharmaceutical use and a process for their preparation.

2. Claims: 7, 8(partly), 9(partly)

   Condensed pyrimidine derivatives of the formula as defined in claim 7 and pharmaceutical compositions comprising them.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern[illegible]al Application No
PCT/US 00/01581

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C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, or $S(O)_2R^{10}$;

Each R^{12} is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN;

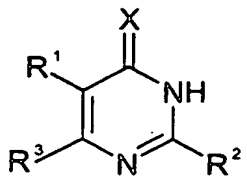
Each R^{15} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^9;

Each R^{16} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; C1-C10 alkyl substituted with 1-3 independent aryl, R^7 or R^9 groups; C1-C10 alkenyl substituted with 1-3 independent aryl, R^7 or R^9; or phenyl substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$, C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$,

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, wherein the number of halogen atoms may not exceed that number that results in a perhaloalkyl group; and

Each aryl is independently a 6-carbon monocyclic or 10-carbon bicyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; CF_3; OR^{12}; SR^{12}; $NR^{12}R^{12}$; $COOR^{12}$; NO_2; CN; $C(O)R^{12}$; $C(O)C(O)R^{12}$; $C(O)NR^{12}R^{12}$; $S(O)_2R^{12}$; $N(R^{12})C(O)R^{12}$; $N(R^{12})(COOR^{12})$; $N(R^{12})S(O)_2R^{12}$; $S(O)_2NR^{12}R^{12}$; $OC(O)R^{12}$; $NR^{12}C(O)NR^{12}R^{12}$; $NR^{12}C(O)C(O)R^{12}$; $NR^{12}C(O)R^9$; $NR^{12}S(O)_2NR^{12}R^{12}$; $NR^{12}S(O)_2R^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; C2-C10 alkenyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; or R^{12}.

2.The compound of claim 1 having the formula:



wherein ,

R^1 is H; $COOR^5$; $C(O)NR^5R^5$; halo; C2-C10 alkyl; C1-C10 alkenyl; C1-C10 alkyl substituted with NR^5R^5, NR^5R^6, SR^5 or OR^5; or C1-C10 alkenyl substituted with NR^5R^5, NR^5R^6, SR^5 or OR^5;

R^2 is NR^5R^{15}; SR^5; OR^5; R^8; aryl; $N(R^5)$-N=CH(R^8); $N(R^5)$-N=CH(aryl); NR^5-$NR^5C(O)NR^5R^5$; NR^5-NR^5R^{16}; NR^5-NR^5R^6; C1-C10 alkyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$; or C1-C10 alkenyl substituted with aryl, R^8, halo, CF_3,

SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$;

R^3 is phenyl substituted with 1-3 independent R^4; R^8; $COOR^5$; or C1-C10 alkyl substituted with aryl, R^7 or R^8;

X is O or S;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, or $S(O)_2R^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, or $C(O)NR^{10}R^{10}$;

Each R^8 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; halo; sulfur; oxygen; CF_3; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; C1-C10 alkyl substituted with R^7, R^9 or aryl; C1-C10 alkenyl substituted with R^7, R^9 or aryl;

Each R^9 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, or $S(O)_2R^{10}$;

Each R^{12} is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN;

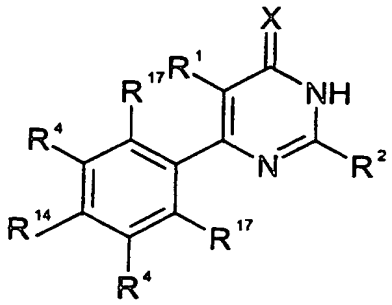
Each R^{15} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^{16} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C1-C10 alkenyl substituted with aryl, R^7 or R^9; or phenyl substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$, C1-C10 alkyl substituted with R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$;

Each R^{19} is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, wherein the number of halogen atoms may not exceed that number that results in a perhaloalkyl group;

Each aryl is independently a 6-carbon monocyclic or 10-carbon bicyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; CF_3; OR^{12}; SR^{12}; $NR^{12}R^{12}$; $COOR^{12}$; NO_2; CN; $C(O)R^{12}$; $C(O)C(O)R^{12}$; $C(O)NR^{12}R^{12}$; $S(O)_2R^{12}$; $N(R^{12})C(O)R^{12}$; $N(R^{12})(COOR^{12})$; $N(R^{12})S(O)_2R^{12}$; $S(O)_2NR^{12}R^{12}$; $OC(O)R^{12}$; $NR^{12}C(O)NR^{12}R^{12}$; $NR^{12}C(O)C(O)R^{12}$; $NR^{12}C(O)R^9$; $NR^{12}S(O)_2NR^{12}R^{12}$; $NR^{12}S(O)_2R^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; C2-C10 alkenyl substituted with



wherein,

R^1 is CN;

R^2 is NR^5R^{15}; OR^5; R^8; aryl; $N(R^5)$-N=CH(R^8); $N(R^5)$-N=CH(aryl); NR^5-$NR^5C(O)NR^5R^5$; NR^5-NR^5R^{16}; NR^5-NR^5R^6; C1-C10 alkyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$; or C1-C10 alkenyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$;

X is O or S;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, or $S(O)_2R^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, or $C(O)NR^{10}R^{10}$;

Each R^8 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; halo; sulfur; oxygen; CF_3; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; C1-C10 alkyl substituted with R^7, R^9 or aryl; C1-C10 alkenyl substituted with R^7, R^9 or aryl;

Each R^9 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, or $S(O)_2R^{10}$;

Each R^{12} is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10

C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN;

Each R^{14} is each independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^{15} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^{16} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C1-C10 alkenyl substituted with aryl, R^7 or R^9; or phenyl substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$, C1-C10 alkyl substituted with R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$;

Each R^{17} is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$;

$C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^{19} is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, wherein the number of halogen atoms may not exceed that number that results in a perhaloalkyl group;

Each aryl is independently a 6-carbon monocyclic or 10-carbon bicyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; CF_3; OR^{12}; SR^{12}; $NR^{12}R^{12}$; $COOR^{12}$; NO_2; CN; $C(O)R^{12}$; $C(O)C(O)R^{12}$; $C(O)NR^{12}R^{12}$; $S(O)_2R^{12}$; $N(R^{12})C(O)R^{12}$; $N(R^{12})(COOR^{12})$; $N(R^{12})S(O)_2R^{12}$; $S(O)_2NR^{12}R^{12}$; $OC(O)R^{12}$; $NR^{12}C(O)NR^{12}R^{12}$; $NR^{12}C(O)C(O)R^{12}$; $NR^{12}C(O)R^9$; $NR^{12}S(O)_2NR^{12}R^{12}$; $NR^{12}S(O)_2R^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; C2-C10 alkenyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; or R^{12};

wherein when all R^4 and R^{17} are simultaneously H, R^{14} may not be Me, Cl, or OMe; and wherein R^{14} and R^{17} may not simultaneously be Cl.

4. The compound of claim 1 having the formula,

wherein,

R^1 is CN;

R^2 is NR^5R^{15}; OR^5; R^8; aryl; $N(R^5)$-N=CH(R^8); $N(R^5)$-N=CH(aryl); NR^5-$NR^5C(O)NR^5R^5$; NR^5-NR^5R^{16}; NR^5-NR^5R^6; C1-C10 alkyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$; or C1-C10 alkenyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$;

X is O or S;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, or $S(O)_2R^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, or $C(O)NR^{10}R^{10}$;

Each R^8 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl;

aryl; R^9; halo; sulfur; oxygen; CF_3; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; C1-C10 alkyl substituted with R^7, R^9 or aryl; C1-C10 alkenyl substituted with R^7, R^9 or aryl;

Each R^9 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, or $S(O)_2R^{10}$;

Each R^{12} is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$

Each R^{14} is independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^{15} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^{16} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C1-C10 alkenyl substituted with aryl, R^7 or R^9; or phenyl substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$, C1-C10 alkyl substituted with R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$;

Each R^{19} is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

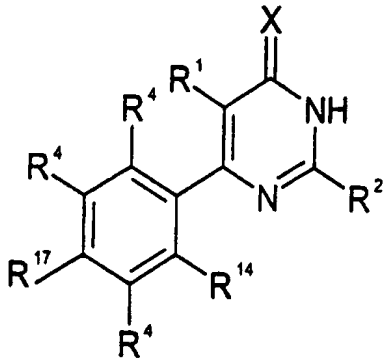
Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, wherein the number of halogen atoms may not exceed that number that results in a perhaloalkyl group;

Each aryl is independently a 6-carbon monocyclic or 10-carbon bicyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; CF_3; OR^{12}; SR^{12}; $NR^{12}R^{12}$; $COOR^{12}$; NO_2; CN; $C(O)R^{12}$; $C(O)C(O)R^{12}$; $C(O)NR^{12}R^{12}$; $S(O)_2R^{12}$; $N(R^{12})C(O)R^{12}$; $N(R^{12})(COOR^{12})$; $N(R^{12})S(O)_2R^{12}$; $S(O)_2NR^{12}R^{12}$; $OC(O)R^{12}$; $NR^{12}C(O)NR^{12}R^{12}$; $NR^{12}C(O)C(O)R^{12}$; $NR^{12}C(O)R^9$; $NR^{12}S(O)_2NR^{12}R^{12}$;

$NR^{12}S(O)_2R^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; C2-C10 alkenyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; or R^{12};

wherein when all R^4 are H, R^{14} may not be Me or OMe.

5. The compound of claim 1 having the formula,



wherein,

R^1 is CN;

R^2 is NR^5R^{15}; OR^5; R^8; aryl; $N(R^5)$-N=CH(R^8); $N(R^5)$-N=CH(aryl); NR^5-$NR^5C(O)NR^5R^5$; NR^5-NR^5R^{16}; NR^5-NR^5R^6; C1-C10 alkyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$; or C1-C10 alkenyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$;

X is O or S;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$;

$NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, or $S(O)_2R^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, or $C(O)NR^{10}R^{10}$;

Each R^8 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; halo; sulfur; oxygen; CF_3; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; C1-C10 alkyl substituted with R^7, R^9 or aryl; C1-C10 alkenyl substituted with R^7, R^9 or aryl;

Each R^9 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-

C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, or $S(O)_2R^{10}$;

Each R^{12} is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN;

Each R^{14} is independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^{15} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted

with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^{17} is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

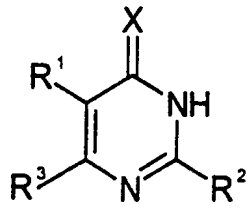
Each R^{19} is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, wherein the number of halogen atoms may not exceed that number that results in a perhaloalkyl group;

Each aryl is independently a 6-carbon monocyclic or 10-carbon bicyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; CF_3; OR^{12}; SR^{12}; $NR^{12}R^{12}$; $COOR^{12}$; NO_2; CN; $C(O)R^{12}$; $C(O)C(O)R^{12}$; $C(O)NR^{12}R^{12}$; $S(O)_2R^{12}$; $N(R^{12})C(O)R^{12}$; $N(R^{12})(COOR^{12})$; $N(R^{12})S(O)_2R^{12}$; $S(O)_2NR^{12}R^{12}$; $OC(O)R^{12}$; $NR^{12}C(O)NR^{12}R^{12}$; $NR^{12}C(O)C(O)R^{12}$; $NR^{12}C(O)R^9$; $NR^{12}S(O)_2NR^{12}R^{12}$; $NR^{12}S(O)_2R^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; C2-C10 alkenyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; or R^{12};

wherein R^{14} and R^{17} may not simultaneously be Cl.

6. The compound of claim 1 having the formula,



wherein ,

R^1 is CN;

R^2 is NR^5R^{15}; OR^5; R^8; aryl; $N(R^5)$-N=CH(R^8); $N(R^5)$-N=CH(aryl); NR^5-$NR^5C(O)NR^5R^5$; NR^5-NR^5R^{16}; NR^5-NR^5R^6; C1-C10 alkyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$; or C1-C10 alkenyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$;

R^3 is R^8; $COOR^5$; or C1-C10 alkyl substituted with R^7, R^8, or phenyl substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$, C1-C10 alkyl substituted with R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; wherein R^3 is not unsubstituted furanyl, unsubstituted thienyl or unsubstituted pyridyl;

X is O or S;

Each R^4 is independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$;

$NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, or $S(O)_2R^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, or $C(O)NR^{10}R^{10}$;

Each R^8 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; halo; sulfur; oxygen; CF_3; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; C1-C10 alkyl substituted with R^7, R^9 or aryl; C1-C10 alkenyl substituted with R^7, R^9 or aryl;

Each R^9 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-

C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, or $S(O)_2R^{10}$;

Each R^{12} is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN;

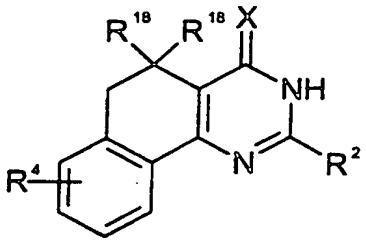
Each R^{15} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^{16} is independently C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C1-C10 alkenyl substituted with aryl, R^7 or R^9; or phenyl substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$, C1-C10 alkyl substituted with R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN $C(O)R^{12}$ $C(O)NR^{12}R^{12}$ $NHC(O)R^{12}$ $NH(COOR^{12})$ $S(O)_2NR^{12}R^{12}$

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, wherein the number of halogen atoms may not exceed that number that results in a perhaloalkyl group;

Each aryl is independently a 6-carbon monocyclic or 10-carbon bicyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; CF_3; OR^{12}; SR^{12}; $NR^{12}R^{12}$; $COOR^{12}$; NO_2; CN; $C(O)R^{12}$; $C(O)C(O)R^{12}$; $C(O)NR^{12}R^{12}$; $S(O)_2R^{12}$; $N(R^{12})C(O)R^{12}$; $N(R^{12})(COOR^{12})$; $N(R^{12})S(O)_2R^{12}$; $S(O)_2NR^{12}R^{12}$; $OC(O)R^{12}$; $NR^{12}C(O)NR^{12}R^{12}$; $NR^{12}C(O)C(O)R^{12}$; $NR^{12}C(O)R^9$; $NR^{12}S(O)_2NR^{12}R^{12}$; $NR^{12}S(O)_2R^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; C2-C10 alkenyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; or R^{12}.

7. A compound of formula,



wherein,

R^2 is NR^5R^5; SR^5; OR^5; R^8; aryl; $N(R^5)$-N=CH(R^8); $N(R^5)$-N=CH(aryl); NR^5-$NR^5C(O)NR^5R^5$; NR^5-NR^5R^{15}; NR^5-NR^5R^6; C1-C10 alkyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$; or C1-C10 alkenyl substituted with aryl, R^8, halo, CF_3, SR^5, OR^5, $OC(O)R^5$, NR^5R^5, NR^5R^6, $COOR^5$, NO_2, CN, $C(O)R^5$, $C(O)NR^5R^5$, or $S(O)_2NR^5R^5$;

X is O or S;

R^4 is one, two, or three substituents, each independently selected from H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^8; halo; haloalkyl; CF_3; SR^5; OR^5; NR^5R^5; NR^5R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)C(O)R^5$; $C(O)NR^5R^5$; $OC(O)R^5$; $S(O)_2R^5$; $S(O)_2NR^5R^5$; $NR^5C(O)NR^5R^5$; $NR^5C(O)C(O)R^5$; $NR^5C(O)R^5$; $NR^5(COOR^5)$; $NR^5C(O)R^8$; $NR^5S(O)_2NR^5R^5$; $NR^5S(O)_2R^5$; $NR^5S(O)_2R^8$; $NR^5C(O)C(O)NR^5R^5$; $NR^5C(O)C(O)NR^5R^6$; C1-C10 alkyl substituted with aryl, R^7 or R^8; or C1-C10 alkenyl substituted with aryl, R^7 or R^8;

Each R^5 is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; C1-C10 alkyl substituted with one or two independent aryl, R^7 or R^9 groups; C3-C10 cycloalkyl substituted with one or two independent aryl, R^7 or R^9 groups; or C1-C10 alkenyl substituted with aryl, R^7 or R^9;

Each R^6 is independently $C(O)R^5$, $COOR^5$, or $S(O)_2R^5$;

Each R^7 is independently halo, CF_3, SR^{10}, OR^{10}, $OC(O)R^{10}$, $NR^{10}R^{10}$, $NR^{10}R^{11}$, $NR^{11}R^{11}$, $COOR^{10}$, NO_2, CN, $C(O)R^{10}$, or $C(O)NR^{10}R^{10}$;

Each R^8 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, which may be saturated or unsaturated, and wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent independently selected from C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; aryl; R^9; halo; sulfur; oxygen; CF_3; haloalkyl; SR^5; OR^5; $OC(O)R^5$; NR^5R^5; NR^5R^6; NR^6R^6; $COOR^5$; NO_2; CN; $C(O)R^5$; $C(O)NR^5R^5$; C1-C10 alkyl substituted with R^7, R^9 or aryl; C1-C10 alkenyl substituted with R^7, R^9 or aryl;

Each R^9 is independently a 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system comprising 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms

C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; halo; sulfur; oxygen; CF_3; haloalkyl; SR^{10}; OR^{10}; $NR^{10}R^{10}$; $NR^{10}R^{11}$; $NR^{11}R^{11}$; $COOR^{10}$; NO_2; CN; $C(O)R^{10}$; or $C(O)NR^{10}R^{10}$;

Each R^{10} is independently H, C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; haloalkyl; C1-C10 alkyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$; or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{11} is independently $C(O)R^{10}$, $COOR^{10}$, or $S(O)_2R^{10}$;

Each R^{12} is independently H, C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, or phenyl optionally substituted with 1-3 independent C1-C10 alkyl, C2-C10 alkenyl, C2-C10 alkynyl, C3-C10 cycloalkyl, C4-C10 cycloalkenyl, halo, CF_3, OR^{13}, SR^{13}, $NR^{13}R^{13}$, $COOR^{13}$, NO_2, CN, $C(O)R^{13}$, $C(O)NR^{13}R^{13}$, $NHC(O)R^{13}$, or $OC(O)R^{13}$;

Each R^{13} is independently H; C1-C10 alkyl; C2-C10 alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; C1-C10 alkyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN; or phenyl optionally substituted with halo, CF_3, OR^{19}, SR^{19}, $NR^{19}R^{19}$, $COOR^{19}$, NO_2, CN;

Each R^{18} is independently C1-C10 alkyl or both R^{18} may be taken together as a C2-C7 alkyl chain; wherein any R^{18} may optionally be substituted with 1-3 independent R^7 or R^8;

Each R^{19} is independently H; C1-C10 alkyl; C3-C10 cycloalkyl or phenyl;

Each haloalkyl is independently a C1-C10 alkyl substituted with one or more halogen atoms, selected from F, Cl, Br, or I, wherein the number of halogen atoms may not exceed that number that results in a perhaloalkyl group;

Each aryl is independently a 6-carbon monocyclic or 10-carbon bicyclic aromatic ring system optionally substituted with 1-3 independent C1-C10 alkyl; C2-C10

alkenyl; C2-C10 alkynyl; C3-C10 cycloalkyl; C4-C10 cycloalkenyl; R^9; halo; haloalkyl; CF_3; OR^{12}; SR^{12}; $NR^{12}R^{12}$; $COOR^{12}$; NO_2; CN; $C(O)R^{12}$; $C(O)C(O)R^{12}$; $C(O)NR^{12}R^{12}$; $S(O)_2R^{12}$; $N(R^{12})C(O)R^{12}$; $N(R^{12})(COOR^{12})$; $N(R^{12})S(O)_2R^{12}$; $S(O)_2NR^{12}R^{12}$; $OC(O)R^{12}$; $NR^{12}C(O)NR^{12}R^{12}$; $NR^{12}C(O)C(O)R^{12}$; $NR^{12}C(O)R^9$; $NR^{12}S(O)_2NR^{12}R^{12}$; $NR^{12}S(O)_2R^9$; $NR^{12}C(O)C(O)NR^{12}R^{12}$; C1-C10 alkyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; C2-C10 alkenyl substituted with 1-3 independent R^9, halo, CF_3, OR^{12}, SR^{12}, $NR^{12}R^{12}$, $COOR^{12}$, NO_2, CN, $C(O)R^{12}$, $C(O)NR^{12}R^{12}$, $NHC(O)R^{12}$, $NH(COOR^{12})$, $S(O)_2NR^{12}R^{12}$, $OC(O)R^{12}$; or R^{12}.

8.A composition comprising a compound according to any of claims 1-7 and a pharmaceutically acceptable carrier.

9. The composition according to claim 8, further comprising an additional therapeutic agent.

10. A method of treating a kinase mediated disease or disease symptoms in a mammal comprising administration to said mammal of a compound of claim 1.

11. The method of claim 10, wherein the mammal is a human.

12. A method of inhibiting kinase activity in a mammal comprising the step of administering to said mammal a compound of claim 1.

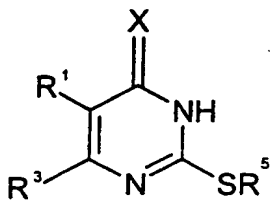
13. The method of claim 12, wherein said mammal is a human.

14. A method of treating disease or disease symptoms in a mammal comprising

16. A method of making a pharmaceutically useful composition comprising combining a compound of claim 1 with one or more pharmaceutically acceptable carriers.

17. The method of claim 16, further comprising combining an additional therapeutic agent.

18. A method of making a compound of claim 1 comprising reacting a pyrimidinone of the formula:



with an appropriate nucleophilic agent, wherein the groups in said formula are as defined in claim 1.

19. The method of claim 18, wherein R^1 is CN; R^3 is phenyl optionally substituted with 1-3 independent R^4; X is O; and R^5 is Me.